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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,845	01/17/2006	Tatsuo Hoshino	21419 US C038435/0185660	2036

7590 09/07/2007

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EXAMINER	
CHOWDHURY, IQBAL HOSSAIN	
ART UNIT	**PAPER NUMBER**
1652	
MAIL DATE	**DELIVERY MODE**
09/07/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/528,845	HOSHINO ET AL.	
	Examiner	Art Unit	
	Iqbal H. Chowdhury, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-15* is/are pending in the application.

4a) Of the above claim(s) *8,12 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4-7, 9-11, 14-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

Claims 1 and 3-15 are currently pending in the instant application.

In response to a previous Office action, a non-final requirement (mailed on 2/28/2007), Applicants filed a response and amendment received on 6/1/2007, amending claims 1, 4, 11, canceling claim 2 and adding new claims 14-15 is acknowledged. Claims 3, 8, and 12-13 remain withdrawn as drawn to nonelected invention.

Claims 1, 4-7, 9-11 and 14-15 are under consideration and will be examined herein.

Applicants' arguments filed on June 1, 2007, have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim objections

Claim 1 and 4 (part (b), line 2) are objected to in the recitation "and hybridizes" which should be "which hybridizes". Appropriate correction is required.

New-Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 4-7, and 9-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite and vague for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 4 are indefinite and vague in the recitation "stringent hybridization and stringent washing condition, but the specification does not define what conditions constitute "stringent hybridization and stringent washing condition.

While page 3 attempts to describe a stringent condition, the description is merely exemplary and not a clear definition. In the art the meaning of the term "stringent" varies widely depending on the individual situation and the person making the determination. Therefore, it is not clear to the Examiner as to what hybridization and washing conditions are encompassed in the above phrase. Accordingly, claims 6-7 and 9-11 are rejected, as they are dependent on claim 1 and 4 respectively.

Maintained - Claim Rejections - 35 U.S.C. § 112

Previous rejection of Claims 1, 4, 7 and 11 under 35 U.S.C. 112, first paragraph, enablement requirement, while the specification being enabling for an isolated DNA with SEQ ID NO: 9, which encodes a polypeptide vitamin B6 phosphate phosphatase enzyme of SEQ ID NO: 10 isolated from S. meliloti, does not reasonably provide enablement for any DNA that is 70% identical to SEQ ID NO: 9 or any DNA encoding a protein having phosphatase activity and having at least 70% identity to SEQ ID NO: 10 or a fragment thereof, is maintained. This rejection has been described in length in previous Office Action. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Applicants argue that Initially, it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling and the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. Applicants also argue that as it is well accepted, even a "considerable amount" of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance and "a patent need not teach, and preferably omits, what is well known in the art" and further argue that that

the specification provides ample disclosure sufficient to inform a skilled artisan that the Applicants enabled the currently claimed vectors, plasmids, and recombinant microorganisms. Furthermore, applicants argue that the specification discloses two examples and four detailed Figures that provide sufficient instruction to one skilled in the art on how to make and use the currently claimed recombinant microorganism, vector, or plasmid encoding vitamin B6 phosphate phosphatase and thus, identifying a recombinant microorganism capable of encoding vitamin B6 phosphate phosphatase according to the amended claims is a matter of applying the disclosure in the specification of how to make such microorganisms and testing the vitamin B6 production of the microorganisms compared to *Sinorhizobium meliloti* IFO 14782.

Applicant's amendment to claim and arguments have been fully considered but are not persuasive to overcome the rejection for the following reasons.

Applicants are silent about scope of any DNA or protein, which is 70% identical to SEQ ID NO: 9 and 10. . The scope of the claimed invention is very broad in the context of at least 70% identity to SEQ ID NO: 9 and 10 i.e. 30% non-identity, wherein 71 amino acids are different out of 235 amino acid residues, which includes many mutants and variants.

As mentioned in the previous Office Actions, claims 1 and 4 are so broad as to encompass any vector comprising a DNA that is 70% identical to SEQ ID NO: 9 or any DNA encoding a protein having at least 70% identity to SEQ ID NO: 10. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of DNAs encoding proteins including mutants, and variants broadly encompassed by the

claims. In the instant case the disclosure is limited to the nucleotide (SEQ ID NO: 9) and encoded amino acid sequence of only a single protein of SEQ ID NO: 10

While methods to produce mutants and variants of a known sequence such as site-specific mutagenesis, random mutagenesis, etc. are well known to the skilled artisan, producing variants useful as vitamin B6 phosphate phosphatase requires that one of ordinary skill in the art know or be provided with guidance for the selection of which of the infinite number of variants have the activity. Without such guidance one of ordinary skill would be reduced to the necessity of producing and testing all of the virtually infinite possibilities. For the rejected claims, this would clearly constitute **undue** experimentation. Guo et al. (Protein tolerance to random amino acid change, Proc Natl Acad Sci U S A, 2004 Jun 22; 101(25): 9205-10, Epub 2004 Jun 14) teach that the percentage of random single substitution mutations which inactivate a protein for the protein 3-methyladenine DNA glycosylase is 34% and that this number appears to be consistent with other studies in other proteins as well. Guo et al. further show in Table 1 that the percentage of active mutants for multiple mutants appears to be exponentially related to this by the simple formula $(.66)^x$ X 100% where x is the number of mutations introduced. Applying this estimate to the instant protein 70% identity allows up to 71 mutations within the 235 amino acids of SEQ ID NO: 10 and thus only $(.66)^{71}$ X 100% or 1.5×10^{-11}% (1 in several billion) of random mutants having 70% identity would be active. Current techniques (i.e., high throughput mutagenesis and screening techniques) in the art would allow for finding a few active mutants within about hundred thousand inactive mutants (despite even this being an enormous quantity of experimentation that would take a very long time to accomplish) but finding a few mutants within several billion or more as in the claims to 70% or less identity would not be possible.

While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. Therefore, for the reasons above, the rejection is maintained.

Withdrawn-Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Previous rejection of Claim 1 under 35 U.S.C. 102(b) as being anticipated by Capela et al. (GenBank Accession No. AL591783 for nucleic acid, created 8/1/2001 see IDS, and GenBank Accession No. Q92SG4, for protein, created 12/1/2001) is withdrawn in view of applicant's amendment of claim 1. Capela et al. do not teach a vector or plasmid comprising said DNA molecule.

Maintained-Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Previous rejection of Claims 2, 4, 7 and 11 under 35 U.S.C. 103(a) as being unpatentable over Capela et al. (GenBank Accession No. AL591783 for nucleic acid, created 8/1/2001 see IDS, and GenBank Accession No. Q92SG4, for protein, created 12/1/2001) and Jang et al. (Human pyridoxal phosphatase. Molecular cloning, functional expression, and tissue distribution, J Biol Chem. 2003 Dec 12; 278(50): 50040-6. Epub 2003 Sep 30) is maintained and now applied to amended claims 1, 4, 7 and 11. This rejection has been discussed at length in the previous Office Action.

Applicants argue that the Examiner fails to identify where in AL591783 it is disclosed that the translation product defined by the polynucleotide sequence encodes

"a vitamin B6 phosphate phosphatase". This is not found persuasive because the protein encoded by the nucleic acid sequence of AL591783 is 99.2% identical to SEQ ID NO: 10 of the instant application, which is **inherently a vitamin B6 phosphate phosphatase protein**. Applicants also argue that Capela does not indicate any function of the polypeptide sequence, and it is simply characterized as a "hypothetical protein." *See* GenBank Accession No. Q92SG4. This is not found persuasive because knowledge of the function is not necessary for motivation and the protein of Capela et al., which is 99.2% identical to SEQ ID NO: 10 of the instant application, inherently has said **vitamin B6 phosphate phosphatase function.** Applicants further argue that the Examiner's assertions are in conflict with his conclusions in the enablement rejection - namely that "even small amino acid changes result in enzymatic activity changes." (Paper No. 20070206 at 10) and further argue that the Examiner cannot have it both ways. This is not found persuasive because the Examiner did not say that the whole disclosure of the instant application is not enabled but a polypeptide which is 70% identical to SEQ ID NO: 10 is not enabled because the polypeptide comprises 30% non-identical amino acid residues i.e. SEQ ID NO: 10 is enabled but not a polypeptide which is 70% identical to SEQ ID NO: 10. Therefore, any polypeptide i.e. Capela et al., which is 99.2% identical to SEQ ID NO: 10 is obvious to one of ordinary skill in the art. Applicants also argue about secondary reference of Jang et al. in 103 rejection, since Capela et al. do not teach cloning said gene in a vector and transform a microorganism E. coli for producing said protein followed by extraction and purification.

As discussed previously, Capela et al. teach a DNA, which encodes a protein that is 99.2% identical to SEQ ID NO: 10 of the instant application, inherently a vitamin B6 phosphate phosphatase protein. Capela et al. do not teach a vector comprising said sequence, transformed

host cell and a method of producing said protein in transformed host cell and extraction of cell lysate.

However, Jang et al. teach human pyridoxal phosphatase or vitamin B6 phosphate phosphatase, its molecular cloning in a vector, functional expression in E. coli host cell, and process for producing said protein followed by extraction and purification (p50041, col1).

It would have been obvious to one to ordinary skill in the art at the time of the invention was made to combine the teachings of Capela et al. and Jang et al. to clone the DNA of Capela et al. by inserting the DNA in a vector, transform an E. coli host cell, a process for producing said protein in E. coli cells, extract the cell lysate and purification by using the teaching of Jang et al.

One of ordinary skill in the art would have been motivated for cloning the DNA of Capela et al. in a vector, transform an E. coli host cell, and a process for producing said protein in said E. coli cell, extract the cell lysate by using the teaching of Jang et al for producing said protein to determine its function by raising antibody of said protein.

One of ordinary skill in the art would have a reasonable expectation of success because cloning a gene, expression and a process for producing said protein is widely known and used in the art for over-producing interested protein in bacterial system. As such the rejection is maintained.

Conclusion

No claims are allowed.

Applicants must respond to the objections/rejections in each of the sections in this Office action to be fully responsive in prosecution. Accordingly, **THIS ACTION IS MADE FINAL**. See M.P.E.P. 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37

C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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